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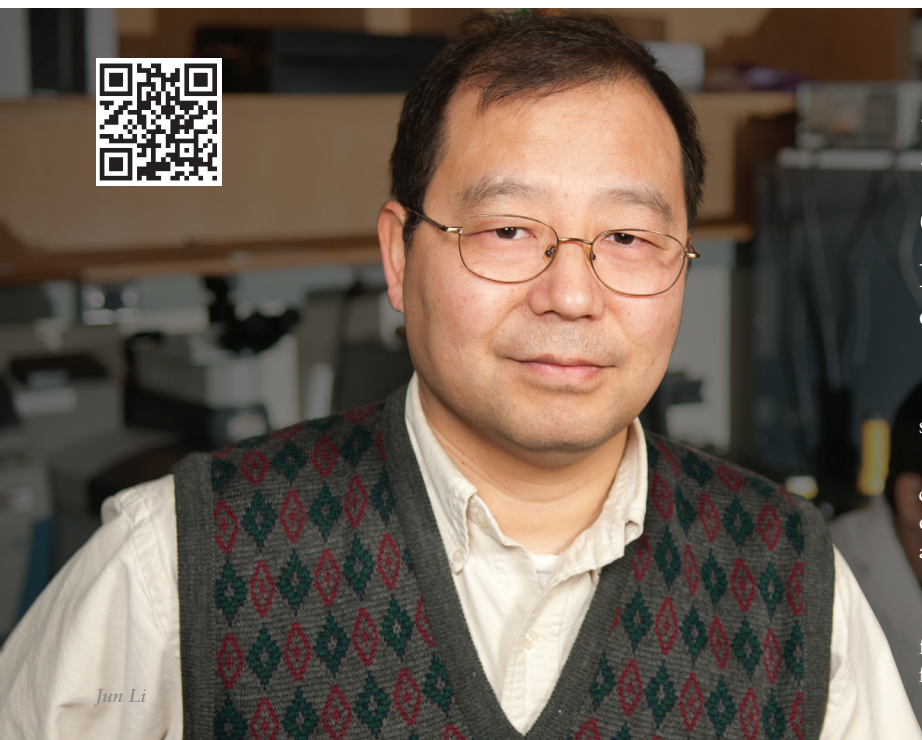
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Perspectives

Spring 2012



Exploring the evidence, cracking the case

How nanotechnology is helping researchers
clue into pathogen, cancer biomarker detection

Several Kansas State University researchers are becoming scientific detectives at the food safety and biomedical scenes.

Under the direction of Jun Li, associate professor of chemistry, they are developing biosensors that can accurately detect even tiny traces of pathogens, blood contamination and cancer cells.

"All of our work centers on nanotechnology," Li said. "It is an exciting area where we can solve health care and food safety problems while protecting lives and preventing financial loss."

Recently, Li and collaborators — including Lateef Syed, a doctoral candidate in chemistry from India — filed a patent for a technique to detect blood contamination. Its commercial potential earned Syed a Kansas State University Research Foundation doctoral research scholarship.

The technique involves attaching chemicals to gold nanoparticles, which light up when blood contamination is detected in a process called chemiluminescence. This method can detect slight traces of biomaterials from less than one blood cell, creating numerous applications for hospitals and crime scene investigations.

"If you spray this material on the computer keyboard or on a doorknob in a hospital, you can see even a slight trace of contamination that otherwise is unnoticeable," Li said. "For crime scene investigations it can chemically trace small amounts of blood, leaving nothing to hide."

Other collaborators include Deryl Troyer, Kansas State University professor of anatomy and physiology, as well as Judy Wu and Mark Richter, both of the University of Kansas. The work was supported by the Institute for Advancing Medical Innovation at the University of Kansas. The institute has filed a provisional patent application for the technique.

A second project for Li and Syed uses carbon nanofibers to create a biosensor chip that detects pathogens such as *E. coli* and salmonella. The goal is to turn this biosensor into an easy-to-use hand-held electronic device.

"It is important for this biosensor to be hand-held because it could immediately analyze a sample on location and determine contamination," Syed said. "This will make it possible to prevent outbreaks through early-stage detection."

Li has been contacted by companies interested in using the biosensor chip. The researchers are now developing the chip to detect viruses, which is important for food safety and biosecurity.

Li and Syed are collaborating on the biosensor chip project with Christopher Culbertson, associate professor of chemistry. Their work has been supported by the Canadian-based company Early Warning Inc., as well as the U.S. Department of Homeland Security through the Center of Excellence for Emerging and Zoonotic Animal Diseases, or CEEZAD, at Kansas State University.

The team has published articles about this work in the journals *Electrophoresis* and *Electroanalysis*. Syed has co-authored two more articles, and the team has a third article submitted.

A third nanobiosensor project by Li is funded by a three-year \$444,000 National Institutes of Health grant. The project focuses on cancer research and early detection of cancer-related enzymes. Cancer patients have enzymes called proteases that tumor cells use to destroy surrounding healthy cells so the tumor has room to grow.

"If we can detect those small concentrations of enzymes as cancer biomarkers in a simpler and faster way, it can show us what stage the cancer is and what treatment should be applied," Li said.

Duy Hua, university distinguished professor of chemistry, and Annelise Nguyen, associate professor of diagnostic medicine and pathobiology, are collaborators for this cancer-related research.

"Our work is quite interdisciplinary," Li said. "We have formed strong collaborative partnerships that allow researchers to build on their strengths and combine their expertise to save the lives of many cancer patients."

— Jennifer Tidball

The new shape of technology

Engineering research uses graphene to form tomorrow's electronics



Graphene research at Kansas State University is taking many shapes: dots, cloaks, ribbons, snowflakes and more.

Vikas Berry, the William H. Honstead professor of chemical engineering, is fabricating these shapes from graphene, a form of carbon that is only one atom thick. He is using it to improve electronics, optoelectronics and computers.

Berry's recent project — supported by a five-year \$400,000 National Science Foundation CAREER award — focuses on graphene quantum dots, which are ultra-small sheets of carbon atoms. Berry's eight-member research team is controlling the size of these graphene particles and shaping them into squares, triangles, rectangles or ribbons. By doing so, they can control graphene's properties over a wide range to develop transistors for future computers, to manipulate graphene-based devices and to engineer novel graphenic nano-systems. The work will be published in an upcoming issue of Nature Communications.

"Several of the graphene quantum dots of shapes — like squares and rectangles — and of defined sizes are unprecedented," Berry said.

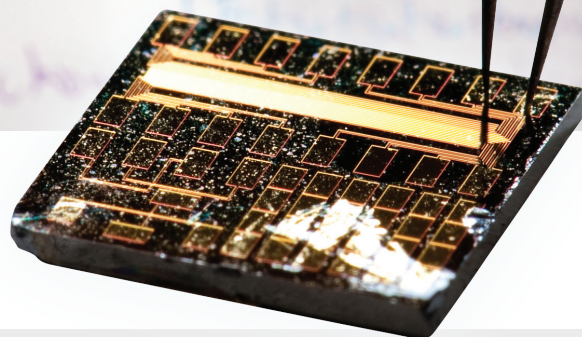
"Our group is the first to synthesize these quantum dots with a wide variety of controlled structure in large quantities. Since their quantum mechanical properties evolve from their shape and size, these quantum dots could be incorporated into several optoelectronic applications, including solar cells."

Because of the high electronic mobility in graphene, it may lead to ultrafast computers, making it a hot topic in the semiconductor industry. Berry has received support from MEMC Electronic Materials, a Missouri-based global supplier of electronic materials to the semiconductor and solar industries, to develop ideas to integrate graphene with silicon. Berry and Mike Seacrist, senior fellow at MEMC, have jointly filed for a patent on this project.

Recently, Berry's team created a microscopic graphene cloak that protects bacteria and other cells under an electron microscope so they can be imaged at their natural size with higher resolution. Their work with graphene cloaks appeared in the journal Nano Letters in 2011. Now the team is using bacterial biochemical processes to create fine wrinkles on the graphene.

"This can be an important breakthrough, since the wrinkles and the associated strain open a band gap in graphene, making it advantageous to fabricate graphene transistors with high rectification," Berry said. "The next step is to compare graphene-devices with and without wrinkles to evaluate the effectiveness of the process for future incorporation into devices."

— Jennifer Tidball



Berry has several other recent projects and accolades related to graphene.

- He has received \$300,000 from the Office of Naval Research to study tapered ribbons of graphene, which have important electrical properties.
- He is currently collaborating with Zhiping Xu from Tsinghua University in China to conduct simulations on the process to produce quantum dots. Berry is also working with Vivek Shenoy from Brown University to study molecular motion on graphene's surface.
- He has a \$301,700 National Science Foundation-funded project on a route to functionalize graphene.
- Berry's team has imbedded gold "snowflakes" on graphene to make it more useful in electronic applications.



The food we eat is under attack by some of nature's tiniest threats. But several plant pathologists at Kansas State University are fighting back both in the field and in the lab.

Anna Whitfield, an associate professor of plant pathology; Dorith Rotenberg, research associate professor in plant pathology; and Bill Bockus, professor of plant pathology, are beginning the second year in a two-year study investigating the diversity of wheat-infecting viruses across the state of Kansas. Kansas is one of the nation's largest wheat producers.

The 2011 wheat season was considered one of the state's worst, with the U.S. Department of Agriculture estimating a 23 percent loss from 2010. But in tandem with brutal combinations of high winds, scorching temperatures and minimal rainfall, researchers found that wheat was also battling a much smaller opponent: viruses.

From April through May 2011, Whitfield, Rotenberg and Bockus — along with Erick De Wolf, associate professor of plant pathology; John Appel, plant pathologist at the Kansas Department of Agriculture, and several student researchers — collected more than 700 samples from 15 wheat variety trials and several commercial fields throughout the state. Samples were analyzed at the university using a process called enzyme-linked immunosorbent assay, or ELISA for short. ELISA uses antibodies to detect viral proteins that may be in the plant tissue.

"We saw that the viruses were very prevalent, very abundant and distributed all over the state last year," Rotenberg said. "We found that more than half of the samples were infected. A portion of those, about 33 percent, were not visually showing symptoms but were infected. Many samples were also infected with more than one virus."

As a result, the team found that 2011's wheat yield was significantly reduced because of viruses — with wheat streak mosaic virus and barley yellow dwarf virus the most prevalent.

The high virus rate could be linked to the warmer and dryer weather causing aphids and other virus vectors to be active during the entire winter. These vector insects could have come into contact with the virus-carrying vegetation and transmitted viruses to 2010's fall wheat crop.

The team is currently collecting and analyzing samples from the same regions in an effort to find whether the viruses differ by region and how they changed from the 2011 year. Heartland Plant Innovations Inc., a Manhattan, Kan.-based company, is supporting the study.

In addition to the wheat virus study, Whitfield and Rotenberg are looking at insect-plant interactions. The focus is how pest insects like thrips and planthoppers spread diseases — such as tomato spotted wilt virus — without getting sick from the disease they carry. By identifying the genes that keep the insect immune, researchers could turn the gene off, ending insects' immunity and consequently reducing the spread of diseases.

"The long-term goal is to either make the insects not able to acquire and transmit the virus or to make the insect susceptible to the virus it's carrying and transmitting," Whitfield said.

Another way to control viruses is by turning the plant against the insect feeding on it.

Whitfield and Rotenberg are developing and testing transgenic tomato plants. The plants have been engineered to express viral proteins. Once a pest insect ingests a part of the plant, the protein will compete with the virus for uptake and potentially prevent the virus from entering the insect.

Another option includes the plant expressing small pieces of nucleic acid matching insect immune response genes. After feeding, the matching nucleic acid goes to work, breaking down the insect's gene that gives it immunity and making the insect susceptible to the disease it would spread to the plant.

"This option opens up new environmentally friendly control strategies for an enormous number of insects we really haven't had that option for," Whitfield said. "Generally, this is about protecting the food supply. That's crucial."

— Greg Tammen

Final transmission

Plant pathologists work to stop plant diseases and the insects that spread them

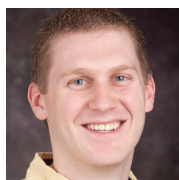


Dorith Rotenberg, Forrest Chumley, Anna Whitfield and Rob Berard (from left to right)

A matter of perspective

Three doctoral students look to new methods and technologies to improve health

A hot topic: Lasers and molecular fingerprinting



Andrew Jones, physics doctoral candidate, Lawrence, Kan., is refining and testing a mid-infrared laser he helped build with Kristan Corwin and Brian Washburn, associate professors of physics.

The laser, the first of its kind, is made from a hollow-core photonic crystal fiber that's about half the width of a human hair. This optical fiber is filled with hydrogen cyanide or acetylene – both molecular gases – and then excited with another laser. One molecule of the excited gas spontaneously emits light, and many others follow suit, resulting in a laser.

"Mid-infrared lasers are pretty hot right now because of all of their applications for molecular fingerprinting – where you want to perform accurate spectroscopic measurements on low concentrations of molecules," Jones said. "For example, for analysis you could breathe into an apparatus and the laser would map out the amount of specific molecules in your breath – useful for diagnosing illness in your body."

A patent application has been filed.

Please check the URL below to watch the video about the laser:
www.ow.ly/9YTYm



For better health: Rats, beetroot juice and fish oil

Steven Copp, doctoral candidate in anatomy and physiology, Manhattan, Kan., and David Poole and Tim Musch, professors of kinesiology and anatomy and physiology, are researching treatments to combat the onset of diabetes, heart

failure and aging by studying rats, beetroot juice and fish oil.

Rats share a similar physiology to humans. The team is observing the treadmill workouts of older rodents with diabetes or heart failure to study the delivery and use of oxygen within the skeletal muscle microvasculature. They are looking at what is responsible for the increases of oxygen delivery and its use in these contracting muscles, as well as how those processes become distorted through diabetes, heart failure and aging.

The rats have an altered nitric oxide function. Nitric oxide is necessary for the function of healthy blood vessels in humans. Researchers are working to correct this altered function through a combination of beetroot juice and fish oil. If successful it would have enormous benefits for humans.

"The overall goal is to be able to take someone who's exhausted from doing things in daily life, like walking across a room, and allow that person to take a walk or play nine holes of golf – just have a dramatically improved quality of life," Copp said.

The eyes have it: Protein may slow tumor growth



Samuel Molina, a doctoral candidate in biochemistry, Mount Pleasant, Mich., is studying the expression of Connexin 46, a protein in the lens of the eye, and how it's regulated by hypoxia, a low oxygen level in tissue that often kills tissue-forming cells.

"The lens is naturally hypoxic and does not have blood vessels. A lot of solid tumors start as hypoxic tumors, meaning they also don't have blood vessels," Molina said. The intent is to find why Connexin 46 provides both lens and tumor cells resistance to hypoxia, which allows them to live longer during hypoxic conditions. By doing so, the growth of tumors could be stopped.

Currently, Molina has found that in samples of breast and retinal tumors in which the Connexin 46 was depleted, the tumor growth and size were reduced. These findings could reduce tumors in the colon and prostate.

Molina's research began under Dolores Takemoto, professor emeritus of biochemistry.

— Greg Tammen

